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EXAMINER

UNDERDAHL, THANE E

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/524,019	Applicant(s) ROCHAT ET AL.	
	Examiner THANE UNDERDAHL	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,8,11,12 and 19-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-6, 8, 11, 12, 19-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

This Office Action is in response to the Applicant's reply received 11/26/08. Claims 1, 3-6, 8, 11, 12, 19-24 are pending. No Claims are withdrawn. Claims 2, 7, 9-10, 13-18 are cancelled. Claims 1 and 3 have been amended. No claims are new.

Response to Applicant's Arguments

In the response submitted by the Applicant the 35 U.S.C § 102 (b) rejection of claims 1, 3, 4, 11, 12, 19-21 and 24 based on Bohr et al. is withdrawn in light of applicant's amendment to claim 2. Also the 35 U.S.C § 103 a rejections of claim 1, 3-6, 11, 12, 19-24 in view of Bohr et al., Plantanias et al. and Rosse et al. and claims 1-6, 8, 11, 12, 19-24 in view of Bohr et al. in view of Cohen et al. have been altered to address the amendment to claim 1.

Revised Rejections under 35 U.S.C § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 11, 12, 19-21 and 24 remain rejected under 35 U.S.C. 103(a) as being obvious over Bohr et al. (U.S. Patent # 6060293) in light of support from 3 entries of Wikipedia (Electric Field, Dielectric Heating, Magnetic Field).

These claims are drawn to a method of stabilizing a recombinant protein solution formulation or recombinant protein-containing solution by storing these solutions under magnetic field lines. The recombinant protein is a physiologically active protein that is isolated and purified selected from the group such as an antibody, enzyme, cytokine and hormone.

Furthermore the claims 19-24 are drawn to stabilizing a composition of a protein in a pharmaceutically acceptable carrier such as water. The proteins for this composition consist of antibodies, enzymes, cytokines and hormones.

Bohr et al. teach a method for stabilizing a recombinant protein solution formulation and solution that contains a recombinant proteins, antibodies as well as enzymes, peptides, and polypeptides under magnetic field lines (see Abstract and col 22, lines 60-65 and col 29, lines 42-51). These proteins are inherently physiologically active since they are used for therapeutic purposes (see Abstract). The method of Bohr et al. can be adapted to a fermentation system for bulk recombinant protein production to reduce the formation of inclusion bodies and their isolation and purification (col 20, lines 25-65 and col 2, lines 20-36). The proteins can be stored under magnetic field lines while in pharmaceutically acceptable carriers such as water (Example 5 and Example 1).

Bohr et al. teach that the amount of energy added or subtracted to the protein solution is critical to the protein stabilization (Bohr, col 39, lines 5-15). Bohr et al. teach that too much electromagnetic energy added to the system will raise the temperature and denature the system and too little energy will also cause denaturation (Bohr, col 39,

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lines 60-65). Indeed while Bohr et al. does not teach that the magnetic flux density of the magnetic field is 1 mT, it would be obvious to one of ordinary skill in the art that adjusting the magnetic flux density would alter the energy imputed into the system which will increase the temperature of the solution and shift the position of the protein in the phase diagram of Bohr et al., possibly denaturing it. This is because one of ordinary skill in the art would know the relationships between the magnetic field strength and power or energy applied to the system which is detailed in the formulas below.

Figure 1-From Wikipedia, Dielectric Heating , pg 2

$$p = \omega \cdot \epsilon_r'' \cdot \epsilon_0 \cdot E^2$$

p = power density

ω = angular frequency

ϵ_r'' = the imaginary part of the complex relative permittivity

ϵ_0 = permittivity of free space

E = electric field strength

Figure 2-From Wikipedia, Electric Field, pg 2

$$\mathbf{E} = \frac{\mathbf{F}}{q}$$

\mathbf{E} = electric field strength

\mathbf{F} = electric force

q = particle charge

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Figure 3-From Wikipedia, Magnetic Field , pg 5

$$\mathbf{F} = q(\mathbf{v} \times \mathbf{B})$$

(\mathbf{v} = instantaneous velocity

\mathbf{B} = magnetic flux density

So by the following formulas the power density of a magnetic field P is directly related to the electric field strength E which is directly related to the magnetic flux density B . So it would be obvious to one of ordinary skill in the art that adjusting the magnetic flux density is one variable that can adjust the power or energy applied to the system which will adjust the temperature. Therefore it would be obvious to one of ordinary skill in the art to carefully and routinely optimize the magnetic flux density applied to the solution so as to not denature the protein. Therefore in the absence of evidence of criticality to the contrary it would be obvious to meet the limitations concerning the magnetic flux density as a matter of routine optimization (M.P.E.P. § 2144.05).

Therefore the reference continues to anticipate claims 1, 3, 4, 11, 12, 19-21 and 24.

Response to Applicant's Arguments

The revised rejection above is meant to address any arguments as to the novelty imparted by the claim limitation "of the magnetic field is 1 mT". The remaining arguments in the response are addressed below.

The Applicant argues that the inventive concept of the current application and Bohr et al. are completely different in scope and thus are not overlapping. As mention

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on pg 2 of the previous Office Action (mailed 8/10/07), when the Examiner is considering the patentability of a method he or she is limited to the steps presented in the claims. In the instant claim 1 the method is for stabilizing a recombinant protein solution formulation by storing said solution under a magnetic field. Indeed this single step is performed by Bohr et al. as stated in previous Office Actions and repeated above.

The Applicant supports their argument further by stating that the claims are to a magnetic field which is constant and that Bohr et al. is to an AC electromagnetic wave (Applicant's Response, Bottom pg 6). Indeed Bohr et al. teach that their applied electromagnetic energy is a "electromagnetic microwave field" (Bohr, col 35, lines 10-15). Also the claims do not limit that the magnetic field be constant or exclude AC magnetic fields. Indeed AC magnetic fields are typically measured in gauss (G) which is directly related to Tesla (T) via a purely numerical constant ($1\text{ T}=10,000\text{ G}$) as supported by TechRentals (See column marked Range) and Online Unit Converter (Magnetic Flux Density). Therefore even AC magnetic fields inherently have a magnetic flux density that is measured in Tesla as supported by TechRentals.

The Applicant asserts that "there is nothing in Bohr regarding storing protein formulation under a magnetic field". The Applicant has not addressed the citations in the above office action that show that Bohr et al. teaches "storing". Indeed Examples 1-6, of Bohr et al. teach that the compound is stored under magnetic fields while the experiments are progressing. The phrase "store" or "storing" is very broad and is not defined or limited by the Applicant. Indeed the duration of how long the formulation is

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stored is not in the claims and a broad reading of such limitation will include any situation where the formulation is placed statically for any amount of time in the magnetic field. Therefor the reference of Bohr et al. still reads on the invention, thus the following 35 U.S.C § 103 rejections that use Bohr et al. as a reference hold as well.

Claims 1, 3-6, 11, 12, 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohr et al as applied to claims 1, 3, 4, 11, 12, 19-21 and 24 above and in further view of rational below with support from Plantanias et al. (JCO, 1991) and further support from Rosse et al. (ASH, Hematology 2000).

While Bohr et al. does store a recombinant protein solution formulation and protein solutions in a pharmaceutically acceptable carrier he does not specifically teach the storage of recombinant hematopoietic factors such as erythropoietin and granulocyte colony-stimulating factor. Regardless this would be obvious to one of ordinary skill in the art by the time the invention was made in view of the teachings of Bohr et al. One of ordinary skill in the art would recognize that recombinant molecules such as recombinant erythropoietin (**EPO**) has been used as a therapeutic agent to treat anemia resulting from chronic renal failure and cancer chemotherapy (as supported by Platantias et al. see abstract) and sickle cell anemia (as supported by Rosse et al. page 8, col 1 paragraph 1 and page 13, col 1 paragraph 3). Since the method of Bohr et al. intends to treat numerous diseases by producing, isolating and stabilizing recombinant proteins by storing them under magnetic field lines, it would have been obvious to someone skilled in the art to produce and stabilized EPO with the

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method of Bohr et al. The motivation is provided by Bohr et al. who expressly desires to treat anemia and cancer (col 27, 43-59) with the proteins produced by their method.

The reasonable expectation of success comes from the successful treatment of anemia with EPO.

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the references listed above and as such claims 1, 3-6, 11, 12, 19-24 are not allowable.

Claims 1, 3-6, 8, 11, 12, 19-24 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bohr et al. as applied to claim 1, 3, 4, 11, 12, 19-21 and 24 above and in further view of Cohen et al. (U.S. Patent # 3308809).

The description and rejection of claims 1, 3, 4, 11, 12, 19-21 and 24 are listed in the 35 U.S.C § 103(a) rejection above. Claim 8 further limits the method of claim 1 by storing the protein solution formulation in a pre-filled syringe.

While Bohr et al. teach applying his method of storing a protein solution formulation to apparatus such as a Fermentor (Bohr, col 20, lines 38-67) they do not teach an apparatus such as a syringe. Regardless this would be obvious to one of ordinary skill in the art by the time the invention was made in view of the teachings of Cohen who teaches a syringe for storing blood specimens from humans in syringes. Since the method of Bohr et al. is for treating blood type diseases such as sickle cell anemia, hemophilia (Bohr col 27, lines 42-59) it would have been obvious to someone skilled in the art to store the protein solution of Bohr et al. in the syringe of Cohen since

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Bohr et al. intends to treat diseases with their method and syringes are an obvious tool for the administration of therapeutic agents into the body.

Therefore the references listed above renders obvious claims 1, 3-6, 8, 11, 12, 19-24.

No claims are currently allowed in this application. This action remains Non-Final because the Examiner did not properly consider the amended claim limitation of "magnetic field is 1 mT" in claim 1 which was a limitation previously presented limitation.

In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651